Subclinical psychopathology and socio-economic status in unaffected twins discordant for affective disorder

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Abstract

Background: The most potent risk factor for affective disorders is a family history of affective disorder but the specific factors that are transmitted in families are unknown. It is possible to investigate the relation between risk factors and affective disorder by using a high-risk design e.g.: a study of the healthy relatives of patients with affective disorders.
Aim: To compare psychopathology and socio-economic status between twins with a co-twin history of affective disorder and twins without.
Methods: In a cross-sectional high-risk case-control study, healthy monozygotic and dizygotic twins with (High-Risk twins) and without (Low-Risk twins) a co-twin history of affective disorder were identified through nation-wide registers. Participants were assessed using semi-structured psychiatric interviews and self-rating of psychopathology.
Results: High-Risk twins had a lower education level, a lower work position and tendency towards being more often unemployed and early retired than the Low-Risk twins. Furthermore, they presented higher rates of subclinical affective symptoms and were more likely to experience a minor psychiatric diagnosis.
Conclusion: Healthy twins with a high genetic liability to affective disorder seem to present lower socio-economic status, higher rates of subclinical affective symptoms and more often experience a minor psychiatric diagnosis than twins with no familial history of affective disorder. It is not possible from the present cross-sectional data to determine the causality of these findings, thus genetic liability to affective disorder, socio-economic status and minor psychopathology seem to have a complex interrelation.
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1. Introduction

Knowledge is sparse of why some people develop an affective disorder and others not. Affective disorders seem to be caused by multiple factors on different levels (physical, psychological, social) (Cuijpers et al., 2005) and several studies have suggested they are a result of an interaction between genetic liability, distress and environmental risk factors (life-events, socio-economic status, poor social skills) (Kendler et al., 1995c; Farmer et al., 2005; Inaba et al., 2005). The exact pathways that lead to disorders are unknown and the specificity of a risk or a protective factor is low. Most individuals exposed to a certain factor do not develop disorder and one risk factor alone is not sufficient to produce the disorder (Rothman and Greenland, 2005). The most potent risk factor for mood disorders is a family history of affective disorder, but the specific factors that are

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transmitted in families are unknown (Mortensen et al., 2003; Merikangas and Low, 2004).

Prospective studies, that measure risk factors before the onset of affective disorder and following successive episodes, provide valid information on the relationship between risk factors and affective disorder (Akiskal et al., 1983). This relation can be examined in two ways: (1) by following psychological healthy persons in a prospective longitudinal population-based design, and (2) by using a high-risk design, a design in which a group of healthy individuals with greater than normal risk for a disorder can be studied cross-sectionally and prospective e.g. the offspring's of affectively ill patients (Goldin et al., 1986). The risk can be increased due to genetic, physiological, behavioural and psychological factors. Population-based studies require many persons to be followed over decades. The high-risk design has the advantage of needing fewer persons to be followed and for a shorter time because of the higher incidence of affective disorder in the group (Christensen and Kessing, 2006).

The aim of this study was to compare psychopathology, somatic health and socio-economic status between a group of healthy twins who have a co-twin history of affective disorder, a High-Risk group, and a group of healthy twins without a family history of affective disorder, a Low-Risk group. Twin studies of bipolar disorder have shown concordance rates from 0.36 to 0.80 in monozygotic twins (MZ) and from 0.04 to 0.19 for dizygotic twins (DZ) (Bertelsen et al., 1977; Kendler et al., 1993b; McGuffin et al., 2003; Kieseppa et al., 2004). A review of studies of unipolar disorder has shown concordance rates from 0.23 to 0.67 for MZ twins and from 0.14 to 0.43 for DZ twins (Sullivan et al., 2000).

Kendler and colleagues (Kendler et al., 1995b) were the first to describe a study design that identified twins in four categories of risk by crossing zygosity with family history of affective disorder. The present study used a new approach in the identification of the cohorts. Thus, healthy MZ and DZ twins with and without at least one first generation family history of affective disorder were identified through nationwide registers. Accordingly, four groups were identified: (1) Twins at high risk for development of affective disorder (MZ twin, co-twin affected). (2) Twins at moderate risk for development of affective disorder (DZ twin, co-twin affected). (3) Twins moderately protected against development of affective disorder (DZ twin, co-twin unaffected). (4) Twins at low risk for development of affective disorder (MZ twin, co-twin unaffected).

Here, we present the basic study design, rate of participation and the results of the cross-sectional comparison of psychopathology, socio-economic status and somatic health.

2. Methods

The first part of the study is a cross-sectional high-risk case-control study. It is planned to follow the participants for five years. The cohort was identified by linkage of the following registers.

2.1. The registers

The Danish Civil Registration System assigns a unique personal identification number for all Danish residents. This number is linked to information on name, address, dates of birth, death, emigration and immigration are recorded in the system. All other Danish registers use the same unique identifier and thus Danish residents can be tracked in all the public registers through record linkage.

The Danish Psychiatric Central Research Register is nationwide, with registration of all psychiatric admissions and outpatients' hospital contacts in Denmark for the country's 5.3 million inhabitants. It contains data on all admissions to Danish psychiatric inpatient facilities, and since 1995 information has been include on outpatient visits to psychiatric departments and community psychiatric centres (Munk-Jorgensen and Mortensen, 1997). From April 1969 to December 1993, diseases were classified according to the International Classification of Diseases, "8th" (ICD-8) (World Health Organization, 1967) and from January 1994, International Classification of Diseases, "10th" (ICD-10) (World Health Organization, 2005).

The Danish Twin Registry was initiated in 1953 and updated on several occasions since then. It now (2005) contains information on 75,000 twin pairs born from 1870 to 2003. The completeness varies with the birth cohort and is approximately 70% for the period before and close to 100% for the period after the Civil Registration System was established (Kyvik et al., 1996; Harvald et al., 2004). The Twin Registry contains information about the zygosity of twins of same-sexed twins based on mailed questionnaires. The questionnaire method used in the Danish Twin Register has been found to result in error rates of less than 5% when compared with serological and DNA methodology (Hauge, 1981; Christiansen et al., 2003).

2.2. The linkage

Through record linkage between the Danish Twin Registry, The Danish Psychiatric Central Research Register and the Danish Civil registration system, a cohort of "High-Risk" twins was identified. This linkage identified 204 twin pairs (same sex, age 22–70 years) in which one twin had been treated in a psychiatric hospital setting for an affective episode (the proband) and one had not been treated for affective